4 Mitochondrial endonuclease G mediates breakdown of paternal mitochondria upon fertilization.

Zhou Q, Li H, Li H, Nakagawa A, Lin JL, Lee ES, Harry BL, Skeen-Gaar RR, Suehiro Y, William D, Mitani S, Yuan HS, Kang BH, Xue D

show author affiliations

Science. 2016 Jul 22; 353(6297):394-9

Recommendations:

Very Good 28 Jul 2016

Youngseok Lee

F1000 Cell Biology

Kookmin University, Seoul, Korea, South.

GOOD FOR TEACHING | NEW FINDING

DOI: 10.3410/f.726446737.793521298

This interesting paper reports on a new candidate CPS-6, mitochondrial endonuclease G, which plays a key role in paternal mitochondrial elimination (PME). The authors performed an RNAi screen with 217 mitochondrial proteins of nuclear genes in C. elegans and analyzed superresolution structured illumination microscope (SIM) images. It had still not been clear before this study why and how paternal mitochondria are selectively eliminated following fertilization. Zhou et al. provide strong evidence that paternal CPS-6, but not maternal CPS-6, relocates from the mitochondrial intermembrane space to the matrix after fertilization to degrade mitochondrial DNA. If paternal CPS-6 is lost, removal of paternal mitochondria can be delayed. In addition, it increases embryonic lethality. This might cause incompatibility in cellular communication between the nuclear and the mitochondrial DNA. This compelling phenomenon should be studied further in the future.

Disclosures
None declared

Add a comment

Very Good 02 Aug 2016

Rosemary Clyne

F1000 Cell Biology

Queen Mary, University of London,
London, UK.

GOOD FOR TEACHING | NEW FINDING

DOI: 10.3410/f.726446737.793521470

The mitochondria and their genome display maternal inheritance: only maternal mitochondria are transmitted to progeny, while paternal mitochondria are eliminated by autophagy. Zhou et al. carried out an RNA interference approach to identify nuclear-encoded mitochondrial proteins involved in this process. The screen revealed CPS-6, the homolog of endonuclease G, as a factor required for elimination of paternal mitochondria after fertilization. Endonuclease G had previously been identified as a mitochondrial DNase that translocates to the nucleus during apoptosis.

CPS-6 is required for the timely degradation of paternal mitochondrial DNA, since loss of cps-6 gene function resulted in its persistence until late stages of embryogenesis. Deletion of the catalytic site of CPS-6 showed a similar effect, confirming that its nuclease activity is required. Furthermore, expression of CPS-6 in the paternal mitochondria is essential for the process, whereas embryos without maternal cps-6 display normal paternal mitochondrial degradation. The CPS-6 protein is predominantly associated with the mitochondrial membrane in spermatozoa, but relocates into the mitochondrial matrix after fertilization.

The findings of Zhou et al. reveal a conserved role for endonuclease G in degradation of paternal mitochondrial DNA after fertilization in animals, and identify a non-apoptotic role for CPS-6 in C. elegans. This elegant series of experiments suggests a model where paternal mitochondria become depolarized following fertilization in this organism, and lose their inner membrane integrity. Autophagy ensues, likely triggered by the relocation of endonuclease G from the intermembrane space into the matrix, where paternal mitochondrial DNA can be degraded.

What factor(s) trigger depolarisation of paternal mitochondria following fertilization with the oocyte? How are paternal mitochondria distinguished from maternal mitochondria? Why does deletion of cps-6 cause embryonic lethality, as Zhou et al. have also shown? Further studies building on this work can begin to probe the mechanism of this intriguing developmental phenomenon.

Disclosures
None declared